New matter has not been introduced by way of amendment. Favorable consideration of the following comments relative to the outstanding rejections as they may apply to the present claims is respectfully requested for the reasons that follow.

Claims 17-20 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite because Claims 17-20 improperly depend from Claim 21. The Examiner contends that Claim 21 does not provide proper antecedent basis for Claims 17-20 and that Claims 17-20, as filed, improperly depend from a higher numbered claim.

In response, Claims 17-20 have been amended to depend from Claim 16. Therefore, Applicants respectfully request the Examiner to withdraw the rejection.

Claims 16-22 stand rejected under 35 U.S.C. § 102(a) and (e). The Examiner contends the disclosure of Mirabelli *et al.* (U.S. Patent No. 5,649,595) of a library of vectors containing random oligonucleotides contained in a population of 2.7×10^8 sequences and mammalian cells containing the vector library anticipate the claimed invention. Applicants traverse the rejection.

The Examiner is respectfully reminded that to anticipate a claim a reference must teach every aspect of the claimed invention either explicitly or impliedly. M.P.E.P. § 706.02(a). In view of this requirement, Applicants assert that Mirabelli *et al.* do not teach a molecular library of retroviruses (Claims 16-20), a cellular library of mammalian cells containing a molecular library of retroviral constructs (Claim 21), or a cellular library in which the retroviral constructs are integrated into a cellular genome (Claim 22).

Regarding the molecular library, Mirabelli *et al.* disclose at column 8, lines 13-42 that suitable expression vectors for construction of a molecular library include double-stranded DNA plasmids such as pMAMM-NEO, pARL100, pYRL100, pMRL100, and ISIS RG-1. It is noteworthy that Mirabelli *et al.* do not teach or suggest a molecular library using any other type of expression vector. The retrovirus molecular library of the present invention is distinct from the plasmid library disclosed by Mirabelli *et al.* in that retroviruses contain an RNA genome which is a component of a nucleoprotein capsid and is encased by a lipoprotein

envelope. Retroviruses also reverse transcribe their RNA genome into DNA which becomes incorporated into the host cell's genome. The expression vectors of Mirabelli *et al.* are circular double stranded DNA that replicate as extrachromosomal elements and, furthermore, are not a component of a retrovirus or any other type of virus particle.

The Examiner has stated that the vectors of Mirabelli *et al.* integrate into a host cell's genome; however, the passage cited by the Examiner (column 15, lines 40-55) does not support this assertion. Column 15, lines 40-55 describes selection of cells expressing oligonucleotides from the disclosed plasmid expression vectors. The passage does not state that the plasmids are incorporated into the host cell's genome or that plasmid expression is dependent upon its incorporation into the cellular genome. Rather, Column 15, lines 51-53 indicates that the plasmid vector is not incorporated into the cellular genome by stating that the plasmid vector may be isolated from the host cells for further analysis.

In view of the absence of a disclosure by Mirabelli *et al.* regarding a molecular library of retroviruses, Applicants assert that Mirabelli *et al.* also do not disclose a cellular library of mammalian cells containing a molecular library of retroviral constructs or a cellular library in which retroviral constructs are integrated into a cellular genome.

Furthermore, Mirabelli *et al.* is directed to the production of antisense nucleic acids, which is distinct from the present claims. For example, Mirabelli *et al.* at column 13, line 64 to column 14, line 1 describe the construction of a vector for the expression of "random and semi-random antisense messages to screen for sequences which specifically inhibit HSV infection of mammalian cells in culture." This approach was also applied to inhibition of the multidrug resistance-associated protein (*see* column 14, line 62 to column 15, line 55) and the *E. coli* beta-galactosidase gene (*see* column 15, line 57 to column 16, line 66). In contrast, the present claims are directed to retroviral libraries that encode a plurality of randomized peptides. Thus, the present invention is fundamentally distinct from Mirabelli *et al.*

Applicants also assert that Mirabelli *et al.* is improperly cited under §102(a). The present application is a divisional of application Serial No. 08/789,333 filed January 23, 1997 which is prior to the issue date of Mirabelli *et al.* of June 17, 1997.

For all of the foregoing reasons, it can be concluded that Mirabelli *et al.* does not anticipate the claimed invention and, therefore, Applicants respectfully request the Examiner to withdraw the rejection.

Claims 16-18 and 21-22 stand rejected under 35 U.S.C. §102(a) as being anticipated by Kitamura *et al.* Applicants traverse the rejection.

Applicants acknowledge that the authorship of Kitamura *et al.* differs from the present inventive entity but assert that the contributions to the Kitamura *et al.* reference by co-authors T. Kitamura, M. Onishi, S. Konishita, A. Shibuya, and A. Miyajima do not rise to the level required of inventorship. Applicants herein submit a Declaration of Garry P. Nolan under 37 C.F. R. §1.132 in accordance with In re Katz attesting to these facts.

The declaration outlines that: i) Dr. Nolan had performed retrovirus vector research while working in the laboratory of Dr. David Baltimore at the Rockefeller University; ii) S. Kinoshita was a post-doctoral fellow working in Dr. Nolan's laboratory at Stanford University, iii) T. Kitamura, M. Onishi, A. Shibuya, and A. Miyajima were world recognized experts at the synthesis of cDNA libraries but had no previous experience with retrovirus vectors; and iv) Dr. Nolan conceived and initiated the research collaboration with T. Kitamura, M. Onishi, S. Kinoshita, A. Shibuya, and A. Miyajima for the expression of a cDNA library using retrovirus vectors.

Therefore, T. Kitamura, M. Onishi, S. Konishita, A. Shibuya, and A. Miyajima were essentially under the direction and supervision of Dr. Nolan in the synthesis of these libraries, and did not contribute to the conception of the invention. Accordingly, T. Kitamura, M. Onishi, S. Konishita, A. Shibuya, and A. Miyajima were co-authors, but not inventors, of the work described in the Kitamura *et al.* reference.

Applicants submit that the enclosed declaration is sufficient to meet the standards of In re Katz, by providing a clear alternative conclusion to the inference that T. Kitamura, M. Onishi, S. Konishita, A. Shibuya, and A. Miyajima were co-inventors.

Therefore, Kitamura *et al.* does not constitute a different inventive entity and is not a proper §102(a) reference.

Even assuming, arguendo, that Kitamura *et al.* was a proper prior art reference, Applicants respectfully assert that Kitamura *et al.* do not anticipate the invention. The present invention is directed to a library of retrovirus vectors comprising randomized nucleic acids. In contrast, Kitamura *et al.* disclose a cDNA library derived from human T-cell clones (*see* page 9147, left column, first full paragraph) and do not teach or suggest a randomized nucleic acid library. Therefore, Kitamura *et al.* do not teach explicitly or impliedly every element of the invention as claimed and neither anticipate nor render obvious the invention as claimed.

In view of these remarks, Applicants respectfully assert that Kitamura *et al.* do not anticipate the claimed invention and respectfully request the Examiner to withdraw the invention.

Claims 16-22 stand rejected under 35 U.S.C. §103, first paragraph as being obvious in view of Kitamura *et al.* Applicants traverse the rejection.

As described above, Applicants submit herein a Declaration of Garry P. Nolan under 37 C.F. R. §1.132 in accordance with In re Katz attesting to the fact that the contributions of co-authors T. Kitamura, M. Onishi, S. Konishita, A. Shibuya, and A. Miyajima were under the direction and supervision of co-author Garry P. Nolan and do not rise to the level required of inventorship. Accordingly, Kitamura *et al.* is not invention "by another" as required by §102(a), and the reference is not a proper prior art reference.

Applicants further submit, for the reasons outlined above in response to the 102(a) rejection, that Kitamura *et al.* do not teach or suggest a retrovirus library comprising randomized nucleic acids. Thus, Kitamura *et al.* do not support a conclusion of obviousness.

In view of these remarks, Applicants respectfully assert that the rejection under 103(a) in view of Kitamura *et al.* is improper and request that it be withdrawn.

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 781-1989.

Respectfully submitted,

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APPENDIX

16. A molecular library of retroviruses comprising at least 10^4 different randomized nucleic acids encoding a plurality of randomized peptides.

17. (Amended) A molecular library of retroviruses according to claim [21]16 comprising at least 10^5 different randomized nucleic acids encoding a plurality of randomized peptides.

18. (Amended) A molecular library of retroviruses according to claim [21]16 comprising at least 10^6 different randomized nucleic acids encoding a plurality of randomized peptides.

19. (Amended) A molecular library of retroviruses according to claim [21]16 comprising at least 10^7 different randomized nucleic acids encoding a plurality of randomized peptides.

20. (Amended) A molecular library of retroviruses according to claim [21]16 comprising at least 10^8 different randomized nucleic acids encoding a plurality of randomized peptides.

21. (Amended) A cellular library of mammalian cells containing a molecular library of retroviral constructs, said molecular library comprising at least 10^4 different randomized nucleic acids encoding a plurality of randomized peptides.

22. A cellular library according to claim 21 wherein said constructs are integrated into the cellular genome.

23. A molecular library of retroviruses according to claim 16, wherein said nucleic acids further encode a fusion partner.

24. A molecular library of retroviruses according to claim 23, wherein said fusion partner comprises a targeting sequence.

25. A molecular library of retroviruses according to claim 23, wherein said fusion partner comprises a rescue sequence.

26. A molecular library of retroviruses according to claim 23, wherein said fusion partner comprises a stability sequence.

27. A molecular library of retroviruses according to claim 23, wherein said fusion partner comprises a multimerization sequence.

28. A molecular library of retroviruses according to claim 16, wherein said randomized nucleic acids are biased in their randomization.